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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,863	11/01/2001	Eric H. Holmes	20093A-002220US	3956

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,863	HOLMES ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48-54 and 63-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-54 and 63-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 48-54, 63-75 are currently pending and are present for examination.

Applicants' amendments and arguments filed on 3-31-04, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically Examiner withdrawn the previous rejections under 35 U.S.C. 112, 1st and 2nd paragraphs in view of claim amendments. Examiner has withdrawn the rejection under Double patenting rules in view of the explanations provided by the applicant.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 53-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 53 recites the phrase having "the nucleotide sequence as depicted as SEQ ID NO:7 and having alpha 1-2 fucosyltransferase activity...". The phrase leads one to believe that the nucleotide sequence itself has the enzyme activity rendering it indefinite because it is well known in the art that nucleotide sequences *encode* polypeptides that may have enzymatic activity. It appears that applicant intended to recite "the nucleotide sequence as depicted as SEQ ID NO:7 *and encoding a polypeptide having* alpha 1-2 fucosyltransferase activity...". If that is so amending the claim accordingly would overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 48-54 and 63-75 are rejected under 35 U.S.C. 102(b) as being anticipated by Holmes et al. (JBC, 1983, Vol. 258(6):3706-3713). This rejection is based upon the public availability of a printed publication. Claims 48-54 and 63-75 of the instant application are drawn to a method of preparation of fucosylated compounds using a fucosyltransferase labeled as α1,2-fucosyltransferase which transfers fucose from GDP-fucose to a molecule having a terminal Galß1→3GalNAc moiety leading to the formation of Fucα1→2Galß1→3GalNAc or which transfers fucose from GDP-fucose to ganglioside GM_1 to form fucosyl-GM_1, wherein said enzyme comprises or consists of an amino acid sequence as depicted in either SEQ ID NO:8 or 10 or encoded by polynucleotide SEQ ID NO:7 or 9. Holmes et al. disclose the isolation and purification of such a fucosyltransferase from rat liver hepatoma and also methods of making the above products using the enzyme. However, the reference does not disclose that the amino acid sequence of the enzyme is either SEQ ID NO:8 or 10 or that it is encoded by a polynucleotide with SEQ ID NO:7. Since the enzyme isolated from Holmes et al. is from rat which has identical properties as that used in the above method, Examiner takes the position that the enzyme used in the claimed method and that disclosed in the reference is one and the same, (i.e., the amino acid sequence of the enzyme in the reference is that of either SEQ ID NO:8 or 10) based on inherency. Amino acid sequence of an enzyme is an inherent characteristic of the

enzyme just as is its functional characteristic. Therefore Holmes et al. anticipate claims 48-54 and 63-75 as written.

Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

In response to the previous Office action, applicant has traversed the above rejection arguing that, for a reference to inherently disclose a claim limitation, the recited limitation must be "necessarily present" in the reference and that Examiner has not set forth sufficient facts to support a *prima facie* case for inherency. Such an argument would hold water, if at least the source of the enzyme in question was different. However, such is not the case. The enzyme used in the claimed methods and the enzyme found n the reference are from the same source. Examiner respectfully disagrees applicant's argument as being persuasive to overcome the rejection. This is because it is primary knowledge in the art that amino acid sequences form polypeptides which go to form enzymes. Therefore, if the reference shows that a specific enzymatic activity has been isolated and purified, it will be well understood by those who practice the art that said specific isolated enzyme comprises an amino acid sequence. Applicant appears to make an unreasonable demand from the Examiner to prove this basic knowledge in order to set forth the inherency argument. Next, applicant argues that Holmes reference discloses a crude homogenate and it cannot be concluded that the activity detected resulted from

a single enzyme or multiple enzymes. Examiner respectfully disagrees that such an argument because, Holmes et al. not only show the specific fucosyltransferase activity, but determine the pH optimum for the reaction and other requirements for the activity such as effect of time and protein concentration, saturation with GDP-Fucose, saturation with GM1 and acceptor specificity. Such studies would not have been possible without a reasonably pure form of the enzyme. Furthermore, irrespective of the purity of the preparation, Holmes et al. demonstrate the same method of fucosylation using a preparation prepared from rat liver as in the instant case. Furthermore applicant's argument that natural isoforms of a given protein exist is rendered moot as applicant's claims are directed to a reaction *comprising* recombinant fucosyltransferase. In support of the inherency argument, Examiner draws the attention of the applicant to another evidentiary reference of Holmes et al. (Archives of Biochem and Biophys, Vol. 355(2):215-221, 1998) in which the inventors have published the full sequence of the enzyme which matches 100% with SEQ ID NO:8. Therefore, for all the above reasons, Examiner continues to maintain the above rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 48-54 and 63-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes et al. (see above), and the common knowledge in the art of protein purification and

molecular cloning techniques. Claims 48-54 and 63-75 are drawn to a method of preparation of fucosylated compounds which method comprises using a recombinant fucosyltransferase labeled as α1,2-fucosyltransferase which transfers fucose from GDP-fucose to a molecule having a terminal Galß1→3GalNAc moiety leading to the formation of Fucα1→2Galß1→3GalNAc or which transfers fucose from GDP-fucose to ganglioside GM_1 to form fucosyl-GM_1, wherein said enzyme comprises or consists of an amino acid sequence as depicted in either SEQ ID NO:8 or 10 or encoded by polynucleotide SEQ ID NO:7 or 9.

The reference of Holmes et al. which teaches the purification of the enzyme from crude rat liver extract has already been discussed above. Holmes et al. teach the purification of the above enzyme up to a point wherein its specific characteristics could be determined. The reference teaches the activity of said enzyme is induced in response to certain signals leading to the formation of specific fucogangliosides in rat livers. Using the above enzyme preparation taught by Holmes et al., it would have been obvious to those skilled in the art to purify the enzyme further using the highly improved protein purification techniques available at the time the instant application was filed, obtain the amino acid sequence and obtain a cDNA clone and arrive at a recombinant enzyme by using the common knowledge available in the art of molecular biology at the time of filing of the instant application. One of ordinary skill in the art would have been motivated to do so because Holmes et al. teach that this enzyme is induced during chemical carcinogenesis and therefore a recombinant form of the enzyme would be very useful for studying its properties extensively and such studies could have tremendous implication in understanding the mechanism of cancer in humans as well. One of ordinary skill in the art would have a reasonable expectation of success since Holmes et al. provide a pure enough

material which can be used for further studies and the art is rich in several techniques and procedures in purifying the protein to homogeneity and obtaining its cDNA to make recombinant proteins. Therefore the above invention would have been *prima facie* obvious to one of ordinary skill in the art.

In response to the previous Office action, applicant has traversed the above rejection arguing that Examiner has not established a proper *prima facie* case of obviousness. In the instant case, applicant argues, Examiner has not established a teaching or suggestion in the prior art for a "recombinant alpha 1,2-fucosyltransferase" as recited in the claims since neither Holmes et al. nor the common knowledge in the art contain any teaching or suggestion of a DNA molecule encoding the respective enzyme. Examiner respectfully disagrees with such line of argument. This is because, there is a general suggestion in the art that making recombinant enzyme has its advantages, especially regarding the ability to obtain uniform quality and large amounts of the recombinant enzyme as opposed to obtaining the enzyme for any purpose by isolating from its natural source. In this case, since the enzyme was isolated from rat livers, obtaining the enzyme in the form of recombinant enzyme leads to avoiding sacrificing rats for their livers.

Next, applicant argues that a cDNA encoding an alpha 1-2 fucosyltransferase having SEQ ID NO:8 or 10 was not known or obvious as of the effective filing date of the instant application and that it is well-established that a DNA molecule encoding a protein is not rendered obvious by general knowledge of methods for obtaining the DNA, even where the protein is known in the art. *In re Deuel*, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995); *In re Bell*, 26 USPQ2d 1529 (Fed. Cir. 1993). Applicant continues, as the Federal Circuit has stated, "in the

absence of other prior art" that suggests specific DNA molecules, "the existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious." *In re Deuel*, 34 USPQ2d at 1215 (reaffirming *In re Bell*, 26 USPQ2d 1529). Here again, Examiner respectfully disagrees with such an argument. Applicants are over-applying the land-mark decisions of the above two court cases. The above court decisions cannot be applied to the instant claims because applicants are not claiming a polynucleotide sequence and Examiner is not rejecting the claims drawn to a polynucleotide sequence. It should be kept in mind that applicant's claims are drawn to a method of use of the polypeptide and therefore using the above argument which mainly applies to a claim directed to a polynucleotide sequence is highly misplaced.

Applicant keeps arguing as if the claims are directed to a process of using a polynucleotide while actually the claims are directed to the method of use of a polypeptide. Based on such tangential arguments, applicant concludes that the polynucleotide encoding the polypeptide was not known and therefore the claims are not obvious.

Next, applicant brings in the question of inherency into the obviousness rejection even though Examiner has not made any such argument in the above rejection. Therefore, all arguments trying to establish that the amino acid sequence is not inherent is rendered moot. In view of all the above, Examiner maintains that claims 48-54 and 63-75 are rendered *prima facie* obvious by the above reference.

Conclusion

None of the claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Manjunath N. Rao Ph.D.
Patent Examiner, A.U. 1652
6/16/04